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TECH CENTER 1600/2900

**DECLARATION FOR
UTILITY OR DESIGN
PATENT APPLICATION**

Attorney Docket No.: 17620/9277

First Named Inventor: Mazess

COMPLETE IF KNOWN☐ Declaration Submitted with Initial Filing☒ Declaration Submitted after Initial Filing

Application Number: 09/402,636

Filing Date:

Group Art Unit:

Examiner Name:

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am first and joint inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled:

TARGETED THERAPEUTIC DELIVERY OF VITAMIN D COMPOUNDS

the specification of which

☐ is attached hereto☒ was filed as United States Application Number 09/402,636.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached?	
				YES	NO
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)
60/038,364	13 February 1997

DECLARATION—Utility or Design Patent Application

I hereby claim the benefit under Title 35, United States Code § 120 of any United States application(s), or § 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of Title 35, United States Code § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

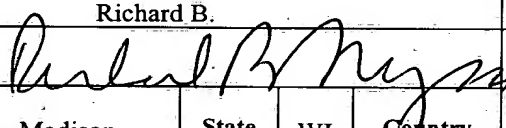
U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (if applicable)
	PCT/US98/02899	February 13, 1998	

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Name	Registration Number
Teresa J. Welch	33,049
Grady J. Frenchick	29,018
Linda Blair Meier	39,769
Paul F. Donovan	39,962
Jill A. Fahrlander	42,518
Karen B. King	41,898
David R. Price	31,557
David B. Smith	27,595
Gregory J. Hartwig	46,761

Direct all correspondence to: Teresa J. Welch
Michael Best & Friedrich LLP
One South Pinckney Street, Suite 700
P. O. Box 1806
Madison, WI 53701-1806
United States of America
Telephone: (608) 257-3501
Fax: (608) 283-2275

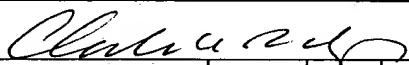
I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statement may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor:					<input type="checkbox"/> A petition has been filed for this unsigned inventor				
Given Name (first and middle [if any])					Family Name or Surname				
Richard B.					Mazess				
Inventor's Signature					Date	7/9/01			
Residence (City)	Madison	State	WI	Country	US	Citizenship	US		
Post Office Address	3534 Blackhawk Drive								
Post Office Address									
City	Madison	State	WI	Zip Code	53705	Country	US		

DECLARATION	Additional Inventor(s) Supplemental Sheet Page 1
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Name of Additional Joint Inventor:

☐ A petition has been filed for this unsigned inventor

Given Name (first and middle [if any])				Family Name or Surname			
Charles W.				Bishop			
Inventor's Signature				Date	July 9, 2001		
Residence (City)	Madison	State	WI	Country	US	Citizenship	US
Post Office Address		5 LaPoint Terrace					
Post Office Address							
City	Madison	State	WI	Zip Code	53710	Country	US

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17620-9277
UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

JANUARY 10, 2001

MICHAEL BEST & FRIEDRICH LLP
TERESA J. WELCH
ONE SOUTH PINCKNEY STREET
P.O. BOX 1806
MADISON, WI 53701-1806

PTAS
Michael Best & Friedrich

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JAN 16 2001

DOCKETING
MADISON, WI

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

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RECORDATION DATE: 11/02/2000

REEL/FRAME: 011220/0122
NUMBER OF PAGES: 3

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

MAZESS, RICHARD B.

DOC DATE: 10/27/2000

ASSIGNOR:

BISHOP, CHARLES W.

DOC DATE: 10/27/2000

ASSIGNEE:

BONE CARE INTERNATIONAL, INC.
ONE SCIENCE COURT
MADISON, WISCONSIN 53711

SERIAL NUMBER: 09402636

FILING DATE: 04/26/2000

PATENT NUMBER:

ISSUE DATE:

SHAREILL COLES, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

11-13-2000

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

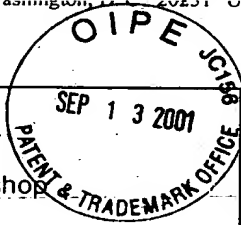
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EL453984537US

Please record the attached original documents or copy thereof.

1. Name of conveying party(ies):
Richard B. Mazess and Charles W. Bishop

2. Name and address of receiving party(ies):

Name: Bone Care International, Inc.

Address:
One Science Court
Madison, WI 53711

3. Nature of Conveyance:

☒ Assignment ☐ Merger
☐ Security Agreement ☐ Change of Name

Other:

Execution Date: October 27, 2000Additional name(s) & address(es) attached? ☐ Yes ☒ No

4. Application number(s) or patent number(s):

A. Patent Application No.(s) 09/402,636
Filed: February 13, 1998

B. Patent No.(s)

Additional numbers attached? ☐ Yes ☐ No

5. Name and address of party to whom correspondence concerning document should be mailed:

Teresa J. Welch
Michael Best & Friedrich LLP
One South Pinckney Street
P. O. Box 1806
Madison, WI 53701-1806

Phone: (608) 257-3501

6. Total number of applications and patents involved:

7. Total fee (37 CFR 3.41):.....\$ 40.00

☒ Enclosed☒ Deficiencies in fee charged to Deposit Account8. Deposit account number: 50-0842

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9. Statement and signature.

*To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.*Jill A. Fahrlander (Reg. No. 42,518)
Name of Person Signing

Signature

November 2, 2000
DateAttorney File 17620-9277

Total number of pages including cover sheet, attachments, and document: 3

OMB No. 0651-0011 (exp. 4/94)

cc: Docketing

Q:\CLIENT\17620\9277\B0031016
11/02/00

ASSIGNMENT

For and in consideration of the sum of One Dollar (\$1.00) to us:

Richard B. Mazess
3534 Blackhawk Drive
Madison, WI 53705

Charles W. Bishop
3 LaPointe Terrace
Madison, WI 53719

paid by Bone Care International, Inc. (hereinafter referred to as "Assignee"), a Wisconsin corporation having its principal place of business at:

One Science Court
Madison, WI 53711

and for other valuable and sufficient consideration, receipt whereof is hereby acknowledged, we hereby sell, assign and convey, unto Assignee, its successors and assigns, our entire right, title and interest -

(1) in and to an invention entitled "TARGETED THERAPEUTIC DELIVERY OF VITAMIN D COMPOUNDS" for which we have executed a United States Application No. 09/402,636, filed February 13, 1998;

(2) in and to said United States patent application, in and to all other patent applications (including divisional, continuation, continuation-in-part, §111(b) provisional, §111(a), and reissue applications) based upon said invention, and in and to the patent or patents to be granted thereon, including reissues thereof, if any, to the full end of the term or terms for which said patent or patents may be granted;

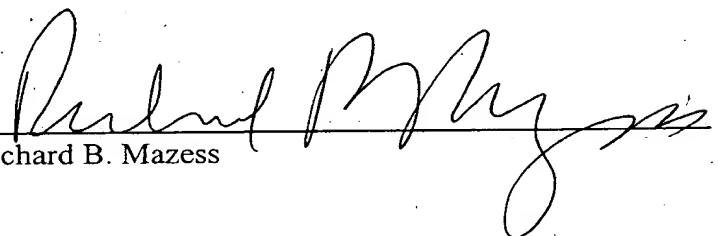
(3) in and to all patent applications on said invention now or hereafter filed in countries foreign to the United States of America, and in and to any and all patents granted on said applications to the full end of the terms for which said patents may be granted; and

(4) under the International Convention in respect to the United States patent application and agree that any patent applications of any foreign countries which may be filed shall be filed in the name of our Assignee with a claim to priority based on said United States application.

And we hereby agree that we will, upon demand of Assignee, its successors or assigns, and without further consideration to us, execute any and all papers that may be necessary, or deemed by Assignee, its successors or assigns, to be necessary, to a complete fulfillment of the intent and purposes of this Assignment, it being understood that any expense incident to the execution of such papers shall be paid by Assignee, its successors and assigns, and not by us.

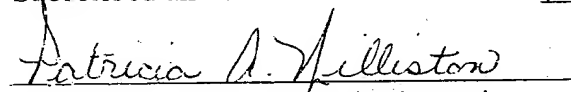
And the Commissioner of Patents and Trademarks of the United States is hereby authorized and requested to issue the said United States patent or patents to Assignee.

Date: 10/27/00

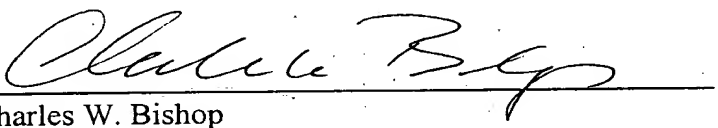

Richard B. Mazess

STATE OF WISCONSIN)
) ss.
COUNTY OF DANE)

Subscribed and sworn to before me this 27th day of October, 2000.

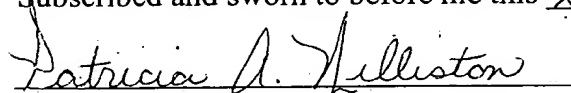

NOTARY Public, State of Wisconsin
My commission expires: 2.29.04

Date: 10/27/00


Charles W. Bishop

STATE OF WISCONSIN)
) ss.
COUNTY OF DANE)

Subscribed and sworn to before me this 27th day of October, 2000.


NOTARY Public, State of Wisconsin
My commission expires: 2.29.04



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Group Art Unit 1644

In re

Patent Application of

Richard B. Mazess, et. al.

Serial No. 09/402,636

Filed: April 26, 2000

Examiner: Phillip Gambel, Ph.D.

"TARGETED THERAPEUTIC DELIVERY OF
VITAMIN D COMPOUNDS"

Diane J. Frauchiger

I, Karen J. Jankowski, hereby certify that this correspondence is being deposited with the US Postal Service as first class mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231, on the date of my signature.

Diane J. Frauchiger
Signature

September 10, 2001
Date of Signature

DECLARATION UNDER 37 C.F.R. 1.132
OF JEFFREY W. DRISCOLL

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

I, Jeffrey W. Driscoll, Ph.D., declare and state the following:

1. I hold the position of Senior Chemist at Bone Care International, Inc., the assignee of the above-identified patent application.

2. I received a Bachelor of Science degree in Chemistry from the University of Wisconsin - Madison in 1983 and a Doctor of Philosophy degree in Chemistry from the University of North Carolina - Chapel Hill in 1993. I have worked in the field of chemistry at least as early as 1993 and in the field of pharmaceutical product synthesis and development at least as early as 1996. From 2000 to the present I have worked in the vitamin D area. My Curriculum Vitae is attached to this declaration and is incorporated herein by reference.

2. I am aware of the relative skill level of those in the art to which the invention disclosed and claimed in the above-identified application pertains. As of the filing date of the application, the ordinary level of skill in the art is a person having a doctorate degree or the equivalent in organic/pharmaceutical syntheses and having specific knowledge of vitamin D chemistry and biochemistry. Thus, the relative level of skill of chemists in the art is quite high. My experience is that of an expert in organic chemical and pharmaceutical synthetic techniques and analyses.

3. Prior to making this declaration, I was given a copy of U.S. Patent Application No. 09/402,636, entitled "Targeted Therapeutic Delivery of Vitamin D Analogues", filed in the U.S. Patent Office on April 26, 2000, claiming priority back to August 13, 1997. I have read and understood the subject application as filed, including the claims. I understand that only claims 1-7, 9, 11, 17, 18 and 20-22 are pending in the application. I have particularly reviewed independent claim 1, which recites a conjugate comprising at least one vitamin D moiety associated with a target molecule moiety having an affinity for a tissue of interest. I have also reviewed independent claim 20, which recites a pharmaceutical composition comprising a conjugate which includes at least one vitamin D moiety associated with at least one target molecule moiety having an affinity for a tissue of interest and a suitable pharmaceutically acceptable carrier.

4. At the same time, I was given a copy of the Office Action dated May 9, 2001. I have reviewed the Office Action and all the references cited by the Examiner, especially the Examiner's assertion that while the specification of the patent application enabled conjugates of vitamin D wherein the vitamin D moiety is linked to various bisphosphonate moieties via an amide linkage, the specification is insufficient with

respect to linkage of the vitamin D moiety to estrogens and their estrogen equivalents and anti-estrogens. Specifically, the Examiner alleges that there is insufficient biochemical information regarding the chemical reaction, the condition to which the reaction will take place, the functional group with the estrogen, antiestrogen and estrogen equivalent structure may be suitable for linking to vitamin D. Thus, the Examiner concludes that predicting which estrogen or antiestrogen will conjugate with vitamin D under unspecified conditions is complex and requires undue experimentation to practice the claimed invention.

5. Based on my experience and my review of the application and the Office Action, I state that the specification of the present applications provides the required guidance and direction to the skilled chemist in the relevant art so that such a chemist would have understood the meaning and breadth of the different claimed conjugates that comprise at least one vitamin D moiety associated with a target molecule moiety having an affinity for a tissue of interest as well as pharmaceutical compositions comprising the same. More particularly, one of ordinary skill would have known how to conjugate target molecule moieties having affinities for a tissue of interest to appropriate vitamin D moieties based on the disclosure. Even more particularly, one having ordinary skill in the art would have known how to select appropriate estrogen or estrogen equivalents as target molecules, bone-targeting molecules, or therapeutic agents. Further, the skilled chemist would have known how to select appropriate connecting groups in order to associate appropriate target molecule moieties with the vitamin D moieties. In my opinion, the disclosure in the present application provides sufficient information to make and use the invention, and making and using the invention would not require undue

experimentation by one of ordinary skill. I have come to this conclusion for the following reasons:

(i) According to the specification of the patent application, the invention described and claimed in the application involves conjugates having at least one vitamin D (designated as "D") moiety associated with at least one target molecule moiety (designated as "T") are represented by formula (I): $D_{(m)} * (T)_n$, wherein n and m represent integers of 1 or greater and * indicates an association between D and T. It is clear from the specification that D represents "at least one vitamin D compound, analog, component or moiety" (page 10, lines 14-15); T represents "at least one target molecule moiety"; and "n and m represent integers of 1 or greater" (page 10, line 17). The specification discloses that it may be desirable to "conjugate hormones or other agents (designated as "A") to the conjugates of formula (I), to form a bifunctional conjugate represented by formula (XV) $(D)_m * (T)_n * (A)_p$, wherein A represents a therapeutic agent other than vitamin D and p is an integer of 1 or greater, D, T, m and n are as previously defined herein, with the proviso that D and A maintain their biological effectiveness" (page 22, lines 3-11). The specification indicates that "a bifunctional conjugate of formula (XV) is one that has the ability to deliver vitamin D to bone as well as another osteogenic agent such as an estrogen" (page 22, lines 11-13).

(ii) More particularly, "D" or "vitamin D" includes all compounds having the conventional vitamin D structure of A, C and D

rings and C-17 side chain as well as previtamin D compounds which are the thermal isomers of their corresponding vitamin D forms, in which the basic structures may be substituted, unsubstituted, or modified" (page 10, lines 21-25). The term "target molecule" or "targeting molecule" "refers to a molecule that binds to or influences metabolism or the tissue of interest" (page 9, lines 12-14). "For example, bone-targeting agents may include bone-seeking molecules such as tetracycline, calcitonin, bisphosphonates, chelators, phosphates, polyaspartic acid, polyglutamic acid, ... estrogens and other steroids such as dehydroepiandrosterone (DHEA)" (page 9, lines 14-22).

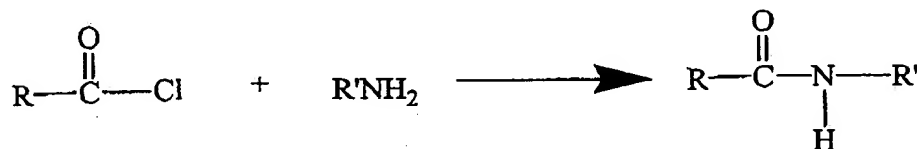
(iii) The terms "associated with" or "association" are clearly defined in the specification: these terms refer to "attachment of linkage of one component of the conjugate (e.g. the vitamin D moiety) or vitamin D moiety and connector to another component of the conjugate, e.g., the target molecule or target molecule and connector, via covalent bonding, hydrogen bonding, metallic bonding, van der Waal forces, ionic bonding, coulombic forces, hydrophobic or hydrophilic forces, adsorption or absorption, chelate type association, or any combination thereof" (page 10, line 30 to page 11, line 4).

(iv) The specification further indicates that included within the scope of the present invention are conjugates of formula (XV) which are bone-therapeutic conjugates wherein A is a hormone or other agent which is known to ameliorate bone diseases or disorders. "The term "bone-

therapeutic agent" is used ... to refer to a specific type of therapeutic agent, one which ameliorates bone diseases or disorders when delivered or administered to bone." (page 10, lines 5-9). "Such bone agents may include conjugated estrogens or their equivalents, antiestrogens, calcitonin, bisphosphonates, calcium supplements cobalamin, pertussis toxin, boron, DHEA and other bone growth factors such as transforming growth factor beta, action or bone morphonogenic protein" (page 22, lines 14-21).

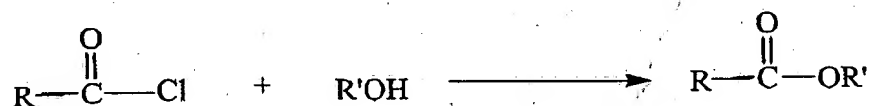
(iv) The specification provides several examples of synthetic schema wherein bone-therapeutic agents, specifically bisphosphonates, are conjugated to a vitamin D moiety. The first step in all of these schema is the reaction of an unprotected hydroxyl group of the vitamin D compound with phosgene, $\text{C}=\text{COCl}$, to form an acyl halide group on the vitamin D compound, e.g., product 2 of the reaction scheme of Figure 1. Acyl halide groups are well known in the art as being very reactive functional groups, and reaction with amines and hydroxyls (i.e., alcohol groups) are some of the most well known organic synthetic reactions.

The acylation of amines by acyl halides yields amides or an amide linkage. This general reaction, exemplifying acyl chlorides, is shown as follows:



As seen in Figure 1 of the specification, the formation of an amide linkage is shown in the reaction of 2 with 3, a bisphosphonate with an amino group, to form an amide linkage, illustrating again the well-known amide formation reaction.

The reaction of acyl halide groups with hydroxyl groups yields carboxylic esters or an ester linkage. This general reaction is shown as follows:

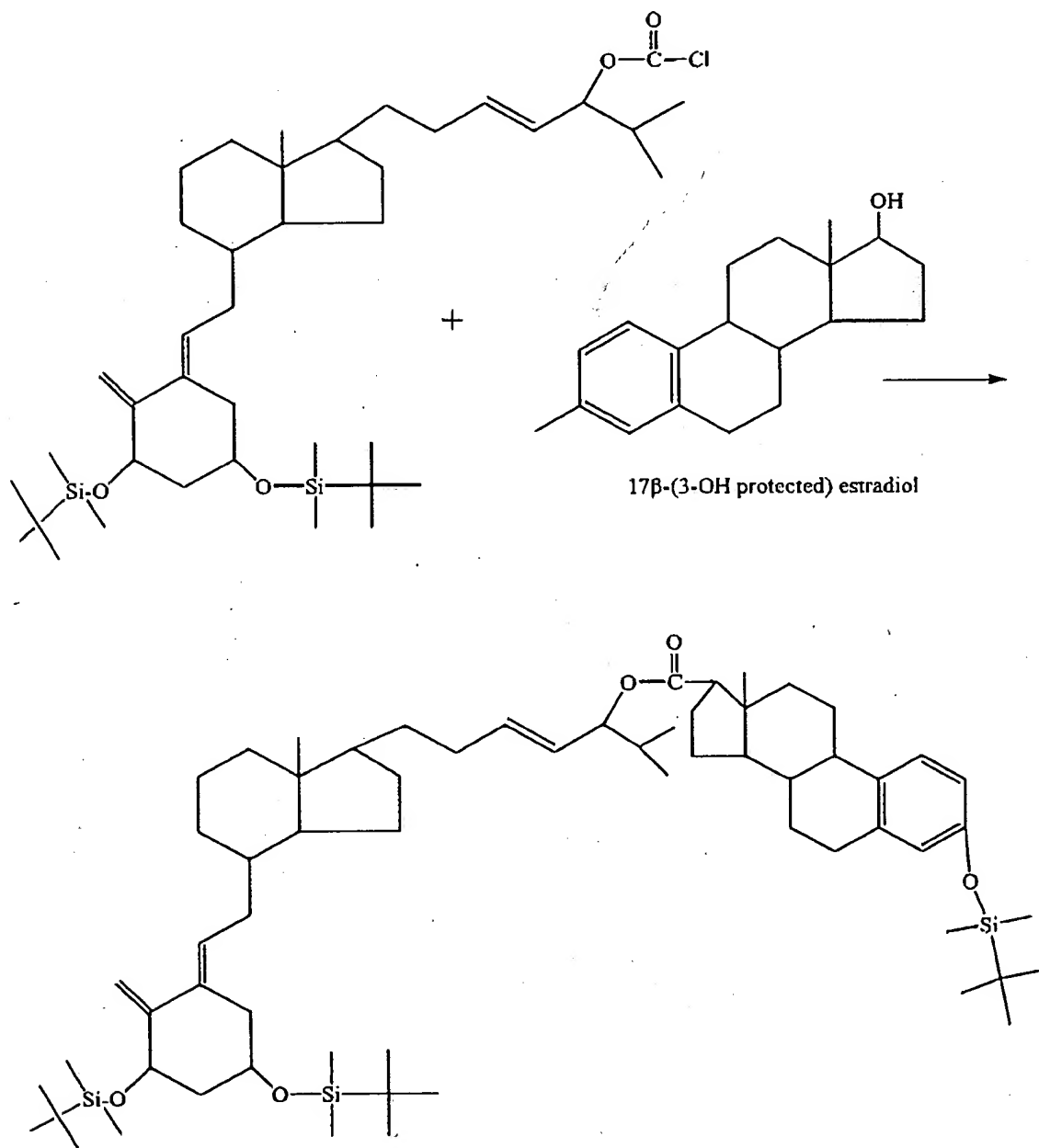


In fact, the alcoholysis of acyl halides, i.e., the reaction between acyl halides and alcohols, is one of the best general methods for the preparation of esters. (See, pages 346 and 370, J. March, Advanced Organic Chemistry, John Wiley & Sons (1985), copy attached hereto.)

The latter reaction is particularly pertinent to the formation conjugates of vitamin D (the vitamin D having a highly reactive acyl halide, e.g., acyl chloride, group) with the hydroxyl groups of, e.g., estrogens. A common estrogen is 17 β -estradiol, a compound that has 2 hydroxyl groups. Either of these hydroxyl groups could react with the acyl chloride of, e.g., vitamin D acyl chloride (product 2), to form a ester linkage, and thus a vitamin D-estrogen conjugate. (It is noted that an unreacted hydroxyl group or any other functional group that would react with the acyl chloride would have a protecting group as shown in the

reaction below.) The reaction of 17 β -estradiol as the estrogen and product

2 as the vitamin D reactant is shown below:



Using the guidance of the bisphosphonate conjugate synthetic schema and knowledge of these general reactions well known in the art, one of ordinary skill in the art would have known how to conjugate a vitamin D moiety with an estrogen, estrogen equivalent or the other disclosed target molecules to form the claimed conjugates and pharmaceutical compositions as of the filing date of the present application. In other words, to make the claimed conjugates and compositions, the specification describes known synthetic techniques. These conjugation techniques, e.g., the formation of an amide linkage or an ester linkage using acyl halide groups, have been known for decades.

6. The claimed invention relies on synthetic technologies known at the time of the filing date of this application. The description of the invention is of sufficient detail and comprehensiveness that chemists knowledgeable in the required field could have made the conjugates and pharmaceutical compositions of the invention as of the date of the filing of the patent application. As a result, it is my opinion that one of ordinary skill in the art would have understood from the syntheses of bisphosphonate conjugates and related references that vitamin D can be linked with any of the target molecules that have an amine or a hydroxyl group.

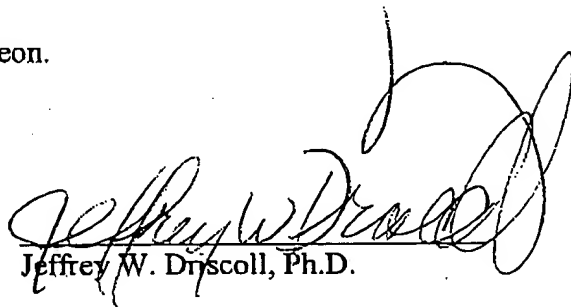
7. In conclusion, from reading the specification alone, or combining the disclosure therein with what was generally known in the art at the time the application was filed, I believe sufficient biochemical information relating to the chemical reactions, the condition by which the reactions take place, and the functional groups that provide suitable linkage between estrogen, antiestrogen, estrogen equivalent structures and other

target molecules to vitamin D was provided in, or could be easily extrapolated from, the specification so that the skilled chemist could practice the claimed invention. Moreover, I believe that no undue experimentation would be required by one of ordinary skill in the art to determine which estrogen, anti-estrogens or target molecules will conjugate with vitamin D.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statement may jeopardize the validity of the application or any patent issued thereon.

Date:

Sept 6, 2001


Jeffrey W. Driscoll, Ph.D.



Jeffrey W. Driscoll
7430 Meadowrue Circle
Middleton, WI 53562

Summary: 18 years post-baccalaureate experience in research, management and education. Experience in physical, analytical and organic chemistry within the chemical and pharmaceutical communities. Thorough understanding of cGMP regulations. Excellent teamwork, multitasking and communication skills.

Work Experience: Bone Care International

Senior Chemist

September, 2000 – Present

- Developed analytical assays in support of preclinical development
- Streamlined departmental operations by organizing equipment and consumables into a computer based system
- Designed and implemented experiments in support of patent work
- Provided company wide support with OSHA regulations as a member of the Safety Committee
- Designed and executed experiments in support of FDA requirements of company's final product

Custom Synthesis Services

Senior Scientist

May 1998 to September 2000

- Designed and implemented multi-step organic syntheses of active drugs and metabolites for the pharmaceutical industry
- Organized the company's synthetic database into a computer based system
- Trained personnel in the procedures and mechanics of successfully searching Beilstein and the Chemical Abstracts systems for chemical information

Wisconsin Analytical and Research Services /Pharmaceutical Product Development

Scientist, Analytical Reference Standards
and Controlled Substances

January 1996 to May 1998

- Responsible for Analytical Reference Standards Program for Bioanalytical and Product Analysis Division
- Responsible for managing outside sourcing of standards from custom synthesis labs, including negotiating contracts and tracking orders to delivery
- Member of the Safety Committee

Aldrich Chemical Company

Quality Control Scientist

September 1993 to November 1995

- Responsible for release of products by review of analytical data in the Quality Control laboratories
- Developed HPLC methods for the separations of stereoisomers
- Developed methods for process control of deuteration experiments using on-line IR spectroscopy
- Member of the Safety Committee



Education: **University of North Carolina at Chapel Hill**
Ph.D., Chemistry, 1993
M.Sc., Chemistry, 1990

University of Wisconsin-Madison
B.S., Chemistry, 1983

Other Affiliations

United States Naval Officer, 1983 to 1988
American Chemical Society
American Association of Pharmaceutical Scientists
Adjunct Professor of Chemistry, Edgewood College



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UNITED STATES DEPARTMENT OF COMMERCE
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ASSISTANT SECRETARY AND COMMISSIONER
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Washington, D.C. 20231

OCTOBER 04, 1995

PTAS



100021078A

MARGARET M. LISS
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25 WEST MAIN STREET
SUITE 300, P.O. BOX 2236
MADISON, WI 53701-2236

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RECORDATION DATE: 04/03/1995

REEL/FRAME: 7498/0210
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BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

KNUTSON, JOYCE C.

DOC DATE: 04/03/1995

ASSIGNOR:

MAZESS, RICHARD B.

DOC DATE: 04/03/1995

ASSIGNOR:

BISHOP, CHARLES W.

DOC DATE: 04/03/1995

ASSIGNEE:

BONE CARE INTERNATIONAL, INC.
313 WEST BELTLINE HIGHWAY
MADISON, WISCONSIN 53713

SERIAL NUMBER: 08415488
PATENT NUMBER:

FILING DATE: 04/03/1995
ISSUE DATE:

SHIRLIE SIMON, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

<p>MAIL ROOM 43-95</p> <p>FORM 1-31-95 1595</p> <p>1-31-95 1995</p> <p>U.S. PATENT & TRADEMARK OFFICE</p>	<p>06-23-1995</p> <p>100021078</p>	<p>U.S. DEPARTMENT OF COMMERCE</p> <p>Patent and Trademark Office</p> <p>08/415488</p> <p>attached original documents or copy thereof.</p>			
<p>To the Patent Commissioner of</p>					
<p>1. Name of conveying party(ies): 71629 U.S. PTO</p> <p>Joyce C. Knutson</p> <p>Richard B. Mazess</p> <p>Charles W. Bishop</p> <p>06/21/95</p> <p>Additional name(s) of conveying party(ies) attached? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>	<p>2. Name and address of receiving party(ies):</p> <p>Name: <u>Bone Care International, Inc.</u></p> <p>Internal Address: <u>313 West Beltline Highway</u></p> <p>Street Address: <u>313 West Beltline Highway</u></p> <p>City: <u>Madison</u> State: <u>WI</u> ZIP: <u>53713</u></p> <p>Additional name(s) & address(es) attached? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>				
<p>3. Nature of conveyance:</p> <p><input checked="" type="checkbox"/> Assignment <input type="checkbox"/> Merger</p> <p><input type="checkbox"/> Security Agreement <input type="checkbox"/> Change of Name</p> <p><input type="checkbox"/> Other</p> <p>Execution Date: <u>April 3, 1995</u></p>					
<p>4. Application number(s) or patent number(s):</p> <p>If this document is being filed together with a new application, the execution date of the application is: <u>April 3, 1995</u></p> <table style="width: 100%;"> <tr> <td style="width: 50%;">A. Patent Application No.(s)</td> <td style="width: 50%;">B. Patent No.(s)</td> </tr> </table> <p>Additional numbers attached? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>			A. Patent Application No.(s)	B. Patent No.(s)	
A. Patent Application No.(s)	B. Patent No.(s)				
<p>5. Name and address of party to whom correspondence concerning document should be mailed:</p> <p>Name: <u>Margaret M. Liss</u></p> <p><u>Stroud, Stroud, Willink, Thompson & Howard</u></p> <p>Internal Address: <u>25 West Main Street,</u></p> <p><u>Suite 300</u></p> <p><u>P.O. Box 2236</u></p> <p><u>Madison, WI 53701-2236</u></p> <p>Street Address: <u>25 West Main Street,</u></p> <p><u>Suite 300</u></p> <p><u>P.O. Box 2236</u></p> <p>City: <u>Madison</u> State: <u>WI</u> ZIP: <u>53701-2236</u></p>	<p>6. Total number of applications and patents involved: <u>1</u></p> <p>7. Total fee (37 CFR 3.41):.....\$40.00</p> <p><input checked="" type="checkbox"/> Enclosed</p> <p><input type="checkbox"/> Authorized to be charged to deposit account</p> <p>8. Deposit account number:</p> <p>(Attach duplicate copy of this page if paying by deposit account)</p>				
DO NOT USE THIS SPACE					
<p>9. Statement and signature.</p> <p><i>To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.</i></p> <table style="width: 100%;"> <tr> <td style="width: 40%;"> <p><u>Margaret M. Liss</u></p> <p>Name of Person Signing</p> </td> <td style="width: 30%; text-align: center;"> <p><u>Margaret M. Liss</u></p> <p>Signature</p> </td> <td style="width: 30%; text-align: right;"> <p><u>April 3, 1995</u></p> <p>Date</p> </td> </tr> </table> <p>Total number of pages comprising cover sheet: <u>3</u></p>			<p><u>Margaret M. Liss</u></p> <p>Name of Person Signing</p>	<p><u>Margaret M. Liss</u></p> <p>Signature</p>	<p><u>April 3, 1995</u></p> <p>Date</p>
<p><u>Margaret M. Liss</u></p> <p>Name of Person Signing</p>	<p><u>Margaret M. Liss</u></p> <p>Signature</p>	<p><u>April 3, 1995</u></p> <p>Date</p>			
<p>OMB No. 0651-0011 (exp. 4/94)</p> <p>020 DC 04/13/95 08415488</p> <p>Do not detach this portion</p> <p>1 581 40.00 CK</p>					
<p>Mail documents to be recorded with required cover sheet information to:</p> <p style="text-align: center;">Commissioner of Patents and Trademarks Box Assignments Washington, D.C. 20231</p>					
<p>Public burden reporting for this sample cover sheet is estimated to average about 30 minutes per document to be recorded, including time for reviewing the document and gathering the data needed, and completing and reviewing the sample cover sheet. Send comments regarding this burden estimate to the U.S. Patent and Trademark Office, Office of Information Systems, PK2-1000C, Washington, D.C. 20231, and to the Office of Management and Budget, Paperwork Reduction Project (0651-0011), Washington, D.C. 20503.</p>					



ASSIGNMENT

PATENT

WHEREAS, Joyce C. Knutson of 24 North Prospect Avenue, Madison, Wisconsin 53705, Richard B. Mazess of 2526 Gregory Street, Madison, Wisconsin 53711, and Charles W. Bishop of 3641 Okanogan Court, Verona, Wisconsin 53593, (hereinafter "ASSIGNOR") have invented the invention entitled METHOD FOR TREATING AND PREVENTING SECONDARY HYPERPARATHYROIDISM for which application for Letters Patent of the United States has been executed on even date herewith; and

WHEREAS, Bone Care International, Inc. (hereinafter "ASSIGNEE"), a corporation organized and existing under and by virtue of the laws of the State of Wisconsin, and having its principal place of business at 313 West Beltline Highway, Madison, Wisconsin 53713, is desirous of acquiring an interest therein;

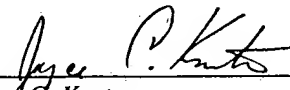
NOW, THEREFORE, in consideration of One Dollar (\$1.00) and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, ASSIGNOR sells, assigns and transfers unto ASSIGNEE, its successors, assigns and legal representatives, the full and exclusive right, title and interest to the inventions as described in the aforesaid application, in the United States and all foreign countries, together with the right of priority under the International Convention for the Protection of Industrial Property, Inter-American Convention Relating to Patents, Designs and Industrial Models, and any other international agreements to which the United States adheres, and in and to all Letters Patent to be obtained for the inventions in the above application and any continuation, division, renewal or substitution thereof and hereby authorize and request the Commissioner of Patents to issue said Letters Patent to ASSIGNEE, for the sole use and benefit of ASSIGNEE, its successors, assigns and legal representatives,

AND HEREBY AGREES to transfer a like interest upon request of ASSIGNEE, its successors, assigns and legal representatives, and without further remuneration, in and to any improvements and applications for patents based thereon, growing out of or relating to the invention; and to provide all reasonable assistance and execute any papers deemed essential by ASSIGNEE, its successors, assigns and legal representatives, to ASSIGNEE's full protection and title in and to the invention hereby transferred,

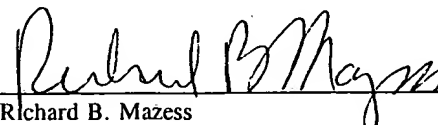
AGREEING, FURTHERMORE, upon request of ASSIGNEE, and without further remuneration, to execute any and all papers desired by ASSIGNEE for the filing and granting of foreign applications and the perfecting of title thereto in ASSIGNEE;

AND HEREBY COVENANTS that no assignment, sale or encumbrance has been or will be made or entered into which would conflict with this assignment.

EXECUTED this 3rd day of April, 1995.



Joyce C. Knutson



Richard B. Mazess



Charles W. Bishop

State of Wisconsin)
) ss.
County of Dane)

On this 3rd day of April, 1995, before me, a notary public in and for said county, appeared Joyce C. Knutson, Richard B. Mazess and Charles W. Bishop, who are personally known to me to be the same persons whose names are subscribed to the foregoing instrument, and they acknowledge that they signed, sealed and delivered the said instrument as their free and voluntary act for the uses and purposes therein set forth.

(Seal)



My Commission Expires: is permanent